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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application of: Aberg *et al.*

Application No.: 09/039,260 Group Art Unit: 1623

Filed: March 16, 1998 Examiner: L. CRANE

For: COMPOSITIONS OF DESCARBOETHOXYLORATADINE Attorney Docket No.: 4821-306

AMENDED BRIEF ON APPEAL

Box PAI
Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In response to the Notice of Non-Compliance dated July 18, 2003 and pursuant to the provisions of 37 C.F.R. § 1.191 and § 1.192, Appellants submit an Amended Brief on Appeal to appeal the final rejection dated October 4, 2001, which rejects claims 48, 50, 52-61 and 63-68 of this application. Appellants submit herewith: (a) an original and two copies of this Amended Brief on Appeal and (b) three copies of each Exhibit cited in the Amended Brief on Appeal.

REAL PARTY IN INTEREST

The real party in interest is the assignee of the above-identified application: Sepracor Inc.

RELATED APPEALS AND INTERFERENCES

Appellants and their legal representatives hereby submit that they are not aware of any appeal or interference which directly affects, will be directly affected by, or will have a bearing on the Board's decision in this appeal.

STATUS OF THE CLAIMS

Claims 48, 50, 52-61 and 63-68 of this application are under final rejection and are the subject of this appeal. Claims 1-14, 49, 51, and 62 were previously canceled. Appellants timely filed a "Notice of Appeal from the Primary Examiner to the Board of Patent Appeals and Interferences" on April 4, 2001. The appealed claims are presented in Appendix A attached hereto.

STATUS OF AMENDMENTS

Subsequent to the October 4, 2000 final Office Action, an amendment under 37 C.F.R. § 1.116 was filed on April 4, 2001. The Examiner indicated that the amendment will be entered upon filing of a Notice of Appeal and an Appeal Brief. Appellants have amended claims 54 and 60 to more clearly recite the claimed invention (Exhibit B). Thus, the claims as presently pending are as set forth in Exhibit A. No new matter has been added by any amendment.

SUMMARY OF THE INVENTION

The invention as recited by the claims on appeal encompasses several distinct and novel pharmaceutical compositions, each comprising descarboethoxyloratadine ("DCL") or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier. However, each composition is distinct in that each also comprises, *inter alia,* an amount of a decongestant (claims 48 and 63-65); acetylsalicylic acid (claim 55); acetaminophen (claim 56); ibuprofen (claim 57); ketoprofen (claim 58); naproxen (claim 59); a non-steroidal anti-inflammatory agent ("NSAID") (claim 66); or a non-narcotic analgesic (claim 67).

At the time the invention was made,[1] DCL was believed to be the major metabolite of the commercially available, non-sedating antihistamine, loratadine (sold as Claritin®). *See* Specification at page 1, lines 5-10. Also at that time, loratadine and other non-sedating antihistamines, such as astemizole and terfenadine, were known to cause severe adverse effects, including ventricular fibrillation and cardiac arrhythmias. *See* Specification at page 3, lines 22-29. However, the invention contemplates the avoidance of such adverse effects, while providing antihistaminic and certain specific therapeutic properties. The pharmaceutical compositions recited by the pending claims are therefore novel and nonobvious.

ISSUES PRESENTED ON APPEAL

1. Whether the deficiencies of U.S. Patent No. 4,659,716 legally can be overcome by combining it with Berkow *et al.*, Merck Manual of Diagnosis and Therapy, 16th Ed., (Merck and Co., Rahway, NJ: May 1992, pp. 324-327 and 2345-2347) to maintain a § 102(b) rejection of claims 48, 50, 52-54, 60-61 and 63-65.

2. Whether the rejection under 35 U.S.C. § 103(a) of claims 48, 50, 52-54, 60-61 and 63-65 over U.S. Patent No. 4,659,716 in view of Berkow *et al.*, Merck Manual of Diagnosis and Therapy, 16th Ed., Merck and Co., Rahway, NJ: May 1992; pp. 324-327 &

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[1] This application is a divisional application of U.S. Application No. 08/783,393, filed January 13, 1997, which issued as U.S. Patent 5,731, 319, which is a divisional application of U.S. Application No. 08/366,651, filed December 30, 1994, which issued as U.S. Patent 5,595,997.

2345-2347 can be maintained despite the failure of the reference to teach or suggest all of the limitations of the claims, despite any motivation to combine these references, and despite the lack of a reasonable expectation of successfully obtaining the claimed invention.

3. Whether the rejection under 35 U.S.C. § 103(a) of claims 55-61 and 66-68 over U.S. Patent No. 4,659,716 in view of Gennaro, Remington's Pharmaceutical Sciences, 18th Ed., Philadelphia College of Pharmacy and Science, 1097-1130 (1990) can be maintained despite the failure of the reference to teach or suggest the limitation of the claims, despite the lack of any motivation to combine these references, and despite the lack of a reasonable expectation of success at obtaining the claimed invention.

GROUPING OF CLAIMS

Claims 48, 50, 52-61, and 63-68 are separately patentable and, according to 37 C.F.R. § 1.192(c)(7), Appellants hereby state that the claims do not stand or fall together. For example, the art generally treats the embodiments encompassed by the claims as distinct (*i.e.*, decongestants, non-steroidal anti-inflammatory agents, non-narcotic analgesics). Other reasons for the separate patentability of these claims is set forth below in the Argument section of this Brief. For purposes of this appeal, the subject claims are herein considered in four (4) different groupings as follows:

Group I: Claims 48, 50, 52-53, and 63-65;
Group II: Claims 54 and 61;
Group III: Claims 55, 57-59, 60-61, 66, and 68; and
Group IV: Claims 56, 60-61, and 67-68.

The claims of Group I are directed to pharmaceutical compositions comprising from about 0.1 mg to about 5 mg of DCL, or a pharmaceutically acceptable salt thereof, an amount of a decongestant, and a pharmaceutically acceptable carrier.

The claims of Group II are directed to pharmaceutical compositions comprising from about 0.1 mg to about 5 mg of DCL, or a pharmaceutically acceptable salt thereof, an amount of a pseudoephedrine, and a pharmaceutically acceptable carrier.

The claims of Group III are directed to pharmaceutical compositions comprising DCL, or a pharmaceutically acceptable salt thereof, non-steroidal anti-inflammatory agents, and a pharmaceutically acceptable carrier.

The claims of Group IV are directed to pharmaceutical compositions comprising descarboethoxyloratidine, or a pharmaceutically acceptable salt thereof, non-narcotic analgesics, and a pharmaceutically acceptable carrier.

REFERENCES RELIED UPON BY THE EXAMINER

Primary: U.S. Patent No. 4,659,716 ("the '716 patent" or "Villani," submitted herewith as Exhibit C), which issued April 21, 1987, discloses a genus of compounds comprising 7- and 8-(halo or trifluoromethyl)-substituted-6,11-dihydro-11-(4-piperidylidene)-5H-benzo[5,6]cyclohepta-[1,2-b]pyridines, and suggests in a general manner that the compounds can be combined with other therapeutic agents, such as decongestants. The '716 patent does not disclose or suggest any specific decongestants, much less a combination of DCL and a decongestant. Indeed, a pharmaceutical composition comprising a specific amount of DCL and a specific decongestant is not disclosed specifically or otherwise in the '716 patent. Moreover, the '716 patent does not disclose any NSAIDs or non-narcotic analgesics, much less a pharmaceutical composition comprising DCL and one of these agents. Therefore, the rejection the pending claims under anticipation or obviousness is legally improper.

Secondary: Berkow *et al.*, Merck Manual of Diagnosis and Therapy, 16th Ed., (Merck and Co., Rahway, NJ: May 1992, pp. 324-327 and 2345-2347) ("Berkow," submitted herewith as Exhibit D) merely states that an antihistamine-decongestant compositions, some of which contain the decongestant pseudoephedrine, are available. However, Berkow does not disclose a specific antihistamine, much less a non-sedating antihistamine such as DCL, nor a specific antihistamine/decongestant.

Gennaro, Remington's Pharmaceutical Sciences, 18th Ed., Philadelphia College of Pharmacy and Science, 1097-1130 (1990) ("Gennaro," submitted herewith as Exhibit E) is a well-known pharmaceutical reference book comprising 109 chapters, each of which deals with a distinct and diverse area in the pharmaceutical sciences. Gennaro discloses literally thousands of different compounds; however, Gennaro does not disclose or suggest anything about DCL nor pharmaceutical compositions that combine DCL with specific therapeutics.

ARGUMENT

Appellants request that the Board of Patent Appeals and Interferences ("the Board") reverse the Examiner's rejections of the pending claims. As discussed below, the Examiner has erred both as a matter of law and fact. The Examiner has erred not only in improperly combining the references but also in failing to appreciate that the appealed claims

can be distinguished over that combination, since the combination fails to disclose or suggest all of the claim limitations recited by the pending claims.

I. THE CLAIMS ARE NOT ANTICIPATED UNDER 35 U.S.C. § 102(b)

A. THE PROPER LEGAL STANDARD

In order to establish anticipation under 35 U.S.C. § 102(b), a prior art reference must disclose each and every limitation found either expressly or inherently in a single prior art reference. *Celeritas Techs. Ltd. v. Rockwell Int'l Corp.*, 150 F.3d 1354, 1360 (Fed. Cir. 1998); *Standard Havens Prods., Inc. v. Gencor Indus.*, Inc., 953 F.2d 1360, 1369 (Fed. Cir. 1991); *Jamesbury Corp. v. Litton Indus. Products*, 756 F.2d 1556 (Fed. Cir. 1985); *American Hospital Supply v. Travenol Labs.*, 745 F.2d 1 (Fed. Cir. 1984) (holding that prior art is anticipatory only if every element of the claimed invention is disclosed in a single item of prior art). It is legally improper to combine prior art references in order to establish an anticipation rejection. *Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264 (Fed. Cir. 1991) (holding that when more than one reference is required to establish anticipation of the claimed invention, anticipation under § 102 cannot be found). Although an additional reference can be used to interpret an allegedly anticipating reference, that is an additional reference can be used to establish how one of ordinary skill in the art would understand an anticipatory reference, it cannot be used to fill in elements missing from the alleged anticipatory reference. *Ciba-Geigy Corp. v. Alza Corp.*, 68 F.3d 487 (Fed. Cir. 1995), citing *Studiengesellschaft Kohle v. Dart Industries*, 726 F.2d 724, 727 (Fed. Cir. 1984). As will be shown below, the Examiner improperly uses a secondary reference to fill in elements missing from the primary reference.

Nevertheless, the black letter law remains that there must be no difference between the claimed invention and the reference disclosure as viewed by one of ordinary skill in the art. *Scripps Clinic & Research Fdn. v. Genentech*, 927 F.2d 1565, 1576 (Fed. Cir. 1991); *Carella v. Starlight Archery and Pro Line Co.*, 804 F.2d 135, 138 (Fed. Cir. 1986); *RCA Corp. v. Applied Digital Data Systems, Inc.*, 730 F.2d 1440, 1444 (Fed. Cir. 1984) (holding that anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference). Put another way, "[a] claim is anticipated and therefore invalid only when a single prior art reference discloses each and every limitation of the claim." *Glaxo Inc. v. Novapharm Ltd.*, 52 F.3d 1043, 1047, *cert. denied*, 116 S. Ct. 516 (1995) (citations omitted) (emphasis added). In addition, to anticipate, the reference must also enable one of skill in the art to make and use the claimed invention. *Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.*, 246 F.3d 1368, 1374 (Fed. Cir. 2001) citing *In re Donohue*, 766 F.2d 531, 533 (Fed. Cir. 1985).

B. CLAIMS 48, 50, 52-53, AND 63-65 ARE NOVEL

Claims 48, 50, 52-53, and 63-65 are directed, in part, to pharmaceutical compositions comprising from about 0.1 mg to about 5 mg of DCL, or a pharmaceutically acceptable salt thereof, an amount of a decongestant, and a pharmaceutically acceptable carrier.

The Examiner rejected claims 48, 50, 52-53, and 63-65 as being anticipated by the '716 patent but relies on Berkow to provide a claim element missing from the '716 patent disclosure. Specifically, Berkow is impermissibly used to provide an example of a specific compound not found anywhere in the '716 patent.[2] An example of the Examiner's improper combination of references under 35 U.S.C. § 102(b) is seen in the Office Actions mailed January 11, 2000 (pages 4-5) and October 4, 2000 (pages 3-5):

> In the Villani reference at col. 8, lines 42-46, the combination of DCL and a decongestant in a single pharmaceutical composition is generically taught. The Berkow reference discloses, at page 326, the combination of an antihistamine with the decongestant "pseudoephedrine" in a single pharmaceutical composition. This teaching represents no more than an exemplification of the generic "antihistamine + decongestant" teaching in the Villani reference.

It is clear that Berkow is not being used to interpret the generic disclosure of the '716 patent but instead is an attempt to add a missing element.[3] *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987); *Atlas Powder Co. v. E.I. DuPont de Nemours & Co.*, 750 F.2d 1569 (Fed. Cir. 1984); *Kalman v. Kimberly-Clark Corp.*, 713 F.2d 760, 771-72 (Fed. Cir. 1983) (holding lack of anticipation under § 102, because the exclusion of a claimed element from a prior art reference is enough to negate anticipation by that reference). If it is necessary to rely upon a second item of prior art to combine with the principal item of prior art in order to complete the teaching of the claim, then the combination of these references will not constitute a § 102 anticipation. *Continental Can Co. USA,* 948 F.2d at 1267 (holding that when more than one reference is required to establish anticipation of the claimed invention, anticipation under § 102 can not be found).

Even if Villani and Berkow could be used to form the basis of a section 102 rejection, that combination does not anticipate any of the pending claims. For example,

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[2] It is well established that the disclosure of a genus does not anticipate a claimed species. *Merck & Co. v. Biocraft Labs., Inc*, 874 F.2d 804, 807 (Fed. Cir. 1989) citing *In re Schaumann*, 572 F.2d 312, 315, 316 (CCPA 1978).

[3] An additional reference can be used only to interpret an allegedly anticipating reference, Berkow was not used in such a way. *Studiengesellschaft Kohle v. Dart Industries*, 726 F.2d 724, 727 (Fed. Cir. 1984).

neither reference discloses explicitly or implicitly each and every limitation of claim 48, which as an exemplary claim, recites a pharmaceutical composition comprising from about 0.1 mg to 5 mg DCL and an amount of a decongestant. *Verdegaal Bros.*, 814 F.2d at 631 (holding lack of anticipation under § 102, because the exclusion of a claimed element from a prior art reference is enough to negate anticipation by that reference).

Villani does not specifically disclose the specific combination of DCL and a decongestant, much less a pharmaceutical composition comprising specific amounts of the specific compound DCL and a decongestant. Villani merely mentions that pharmaceutical preparations can be made which comprise "from 1 mg to 1000 mg" of an "active compound" which can "also contain other therapeutic agents, such as decongestants." Villani, col. 8, lines 42-46. Villani does not point out specific combinations of DCL and a decongestant, much less disclose an amount from about 0.1 to about 5 mg of DCL as recited by the pending claims. Due to the lack of the legally required single item of prior art disclosing each and every element of the claimed invention (*i.e.*, a pharmaceutical composition comprising the specific compound DCL in an amount from about 0.1 mg to 5 mg and an amount of decongestant), the rejection under § 102 is not proper and must be reversed.

Significantly, the amount of DCL recited by claim 48 is drastically less than that which is at best only suggested by Villani. Indeed, Villani suggests a maximum amount of an "active ingredient" which is *10 - 10,000 times* greater than that recited by claim 48. Only about the bottom 1% of the range suggested by Villani can be argued to overlap with that recited by amended claim 48. Consequently, the claimed amount of DCL is not disclosed with "sufficient specificity" by Villani to read on an element of the claimed invention.

> When the prior art discloses a range which touches, overlaps, or is within the claimed range, but no specific examples falling within the claimed range are disclosed, a case by case determination must be made as to anticipation. In order to anticipate the claims, the claimed subject matter must be disclosed in the reference with "sufficient specificity" to constitute an anticipation under the statute. Manual of Patent Examining Procedure. MPEP § 2131.03.

The disclosure by Villani of an amount of active compound varied or adjusted from 1 mg to 1000 mg does not anticipate the specific amount of DCL recited by claim 48. Furthermore, the specific formulations that are disclosed by Villani comprise an "active compound" (wherein "active compound" is defined as "a compound of the invention") in an amount of 100 mg and 500 mg (*i.e.*, 1000 and 100 times greater, respectively, than that recited by the pending claim group). The ranges disclosed by Villani are therefore "so broad as to be meaningless" and provide no guidance on how to construct a product within the

pending claim's range as to provide one of ordinary skill in the art the necessary disclosure to read on the pending claims of group 1. *Minnesota Mining and Manufacturing Co. v. Johnson & Johnson Orthopedics, Inc.*, 976 F.2d 1559, 1572 (Fed. Cir 1992) (holding that a patent must sufficiently describe the claimed invention to have placed the public in possession of it).

For any of the above reasons, the Board should overturn the Examiner's rejection of claims 48, 50, 52, and 53 under 35 U.S.C. § 102(b).

Claims 64 and 65 are also not anticipated by Villani. These claims recite, in part, an aerosol spray and an elixir, respectively, comprising an amount of DCL or a pharmaceutically acceptable salt thereof, and an amount of decongestant.

Anticipation can be found only if a reference discloses exactly what is claimed; where there are differences between the reference disclosures and the claim, a rejection must be based on obviousness under Section 103. *Titanium Metals Corp. v. Banner*, 778 F.2d 775 (Fed. Cir. 1985). An anticipatory reference must also disclose every element of the claim and enable one of ordinary skill in the art to make the subject matter it recites. *PPG Industries, Inc. v. Gaurdian Industries Corp.*, 75 F.3d. 1558 (Fed. Cir. 1996).

Villani does not disclose an aerosol spray or an elixir, much less an aerosol spray or elixir comprising DCL, or a pharmaceutically acceptable salt thereof, and a decongestant. Therefore, the Examiner failed to establish the legally required "identity of invention" between claims 64 and 65 and the cited reference. *Minnesota Mining & Manufacturing Co.* 976 F.2d at 1572.

For this reason, the rejection of claims 64 and 65 under 35 U.S.C. § 102(b) is incorrect and the Board should reverse the Examiner's rejection.

C. CLAIMS 54 AND 61 ARE NOVEL

Claims 54 and 61 are directed to pharmaceutical compositions comprising from about 0.1 mg to about 5 mg of DCL, or a pharmaceutically acceptable salt thereof, an amount of a *pseudoephedrine*, and a pharmaceutically acceptable carrier.

The Examiner rejected claims 54 and 61 under 35 U.S.C. § 102(b) as being anticipated by the '716 patent and Berkow, alleging that Berkow provides the definition of a specific compound well known in the art to be a decongestant. The Examiner alleges that "the combination of an antihistamine with the decongestant 'pseudoephedrine' in a single pharmaceutical composition represents no more than an exemplification of the generic 'antihistamine + decongestant' teaching in the Villani reference." *See* Office Action dated October 4, 2000 at page 4. As discussed above, the Examiner is not using Berkow to interpret the '716 patent but to add a missing element. Referring to Berkow as an exemplification does not negate the illegality of the combination of references under § 102(b).

The invention as recited by claims 54 and 61 is not anticipated by Villani. Independent claim 54 recites a pharmaceutical composition that comprises DCL,

pseudoephedrine, and a pharmaceutically acceptable carrier. Villani does not disclose a specific pharmaceutical composition comprising either DCL or pseudoephedrine, much less a pharmaceutical composition comprising a combination of DCL and pseudoephedrine.[4] Indeed, Villani does not disclose any specific decongestant. *See Verdegaal Bros.*, 814 F.2d at 631 (holding lack of anticipation under § 102, because the exclusion of a claimed element from a prior art reference is enough to negate anticipation by that reference). Villani does not provide a limited list of decongestants but instead merely suggests "decongestants." More important, Villani does not focus its disclosure on decongestants. It instead discloses compositions that "contain other therapeutic agents, such as decongestants." *See* Villani at col. 8, lines 44-46. The vast collection of compounds encompassed by the term "other therapeutics" renders the rejection of claims 54 and 61 under 102(b) over Villani less than credible. Therefore, Villani cannot anticipate a pharmaceutical composition containing DCL and pseudoephedrine.

It is well established that "the disclosure of a chemical genus . . . constitute[s] a description of a specific compound" within the meaning of section 102(b) only where the specific compound falls within the ambit of a "very limited number of compounds." *Merck & Co., Inc., v. Biocraft Laboratories, Inc.*, 874 F.2d 804, 807 (Fed. Cir. 1989) (emphasis added) citing *In re Schaumann*, 572 F.2d 312, 315, 316 (CCPA 1978). This is not true of the '716 patent, particularly with its general reference to "other therapeutics, such as decongestants." Perhaps it is because Villani so clearly fails to anticipate claims 54 and 61 that the Examiner next attempted to combine Villani with Berkow in order to reject claims 54 and 61 under § 102(b).

The Examiner's attempt to expand the disclosure of Villani is not made proper simply because he alleged that Berkow was used "to provide the the definition of a specific compound well known in the art to be a decongestant." *See* October 4, 2000 Office Action at Page 4, lines 1-3. The Examiner does not rely on Berkow to determine the meaning of the term "decongestant" but to find a disclosure of an element missing from Villani. Claims 54 and 61 are therefore not anticipated by Villani.[5]

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[4] The Examiner states that Villani "does not disclose pharmaceutical compositions wherein the specific decongestant has been specified." *See* October 4, 2000 Office Action at page 5, lines 23-26. This admitted failure of the cited reference to disclose a claimed element should by itself obviate the rejection of claims 54, 60, and 61 under § 102(b).

[5] It should be noted that claim 60 further limits the invention to a specific amount of DCL (0.1 to 10 mg), which as stated above is not disclosed inherently or expressly by Villani; thus, the rejection under § 102(b) is improper with respect to claim 60 for this additional reason.

For these reasons, the Examiner's rejections are legally improper, and the Board should therefore reverse the rejection of the claims under § 102(b).

II. REQUIREMENTS FOR ESTABLISHING A *PRIMA FACIA* CASE OF OBVIOUSNESS

Three basic criteria must be met to establish a case of *prima facie* obviousness: first, there must have been at the time of the invention a motivation to combine the references cited. *In re Jones,* 958 F.2d 347 (Fed. Cir. 1992); *In re Fine*, 837 F.2d 1071 (Fed. Cir. 1988) (holding that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves on in the knowledge generally available to one of ordinary skill in the art). Second, the alleged prior art must teach or suggest all of the limitations of the claims alleged to be obvious. *In re Royka,* 490 F.2d 981 (CCPA 1974) (holding that to establish *prima facia* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art); *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991) (holding that the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in the applicant's disclosure). Third, there must have been at the time of the invention a reasonable expectation of success. *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1207-1208 (Fed. Cir.), *cert. denied* 502 U.S. 856 (1991) (holding that to obviousness requires references to show that there was, at the time of the invention, a reasonable expectation of success).

A. THERE MUST BE A SUGGESTION OR MOTIVATION IN THE ART

Both the teaching or suggestion to make the claimed combination and the reasonable expectation of success must be found in the prior art, not in the applicant's disclosure. *In re Deuel*, 51 F.3d 1552, 1558 (Fed. Cir. 1995). Where claimed subject matter has been rejected in view of a combination of prior art references, a proper analysis under § 103 requires, *inter alia*, consideration of: (1) whether the references would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process, and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. *In re Vaeck*, 947 F.2d 488.

B. THE USE OF HINDSIGHT IS NOT PERMISSIBLE

Hindsight cannot be used to reject a claim as obvious. *In re Sernaker*, 702 F.2d 989, 994 (Fed. Cir. 1983); *In re Rinehart*, 531 F.2d 1048 (CCPA 1976); *In re Imperato*, 486 F.2d 585 (CCPA 1973); *In re Adams*, 356 F.2d 998 (CCPA 1966). Consequently, it is insufficient to select from the prior art the separate components of the inventor's combination, using the blueprint supplied by the inventor. *C.R. Bard Inc. v. M3 Systems, Inc.*, 157 F.3d 1340, 1352 (Fed. Cir. 1998) citing *Fromson v. Advance Offset Plate, Inc.*, 755 F.2d 1549, 1556 (Fed. Cir. 1985) (holding the prior art must suggest to one of ordinary skill in the art the desirability of the claimed combination)."

The Federal Circuit has suggested that "the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or modification to combine prior art references." *Id.* This is because "[c]ombining prior art references without evidence of such a suggestion, teaching, or motivation simply takes the inventor's disclosure as a blueprint for piecing together the prior art to defeat patentability — the essence of hindsight." *Id.* (citing *Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 1138 (Fed.Cir. 1985).

C. THE DISCLOSURE OF A GENUS OF COMPOUNDS DOES NOT IN ITSELF TEACH OR SUGGEST THE USE OF A PARTICULAR COMPOUND WITHIN THAT GENUS

The use of impermissible hindsight is particularly attractive during the examination of chemical and pharmaceutical patent applications when a prior art reference discloses a genus of compounds that encompasses a specific compound recited by the claims. However, it is well settled that "[t]he fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious." *In re Baird*, 16 F.3d 380, 382 (Fed.Cir. 1994) (citing *In re Jones*, 958 F.2d 347 (Fed.Cir. 1992). Further, "the fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a *prima facia* case of obviousness." *In re Baird*, 16 F.3d at 382.

IV. THE PENDING CLAIMS ARE NOT OBVIOUS UNDER 35 U.S.C. § 103

The Examiner rejected claims 48, 50, 52-54, 60-61, and 63-65 under 35 U.S.C. § 103 as being obvious over Villani in view of Berkow. The Examiner's rejection in the Office Actions mailed January 11, 2000 and October 4, 2000 is summarized as follows:

> Villani generically discloses the combination of DCL and a decongestant in a single pharmaceutical composition, but the reference does not disclose pharmaceutical compositions wherein the specific decongestant has been specified. *See* Office Actionsat page 5. Berkow discloses the combination of an anti-histamine with the decongestant "pseudoephedrine" in a single

> pharmaceutical composition. However, the reference does not disclose pharmaceutical compositions wherein DCL and any one decongestant have been specified as the active ingredient. Therefore the Examiner alleges that the Villani reference motivates the ordinary practitioner to go out and find a decongestant to combine with DCL in a binary pharmaceutical composition.[6] *See* Office Actions at pages 5-6.

The Examiner also rejected claims 55-62 under 35 U.S.C. § 103 as being obvious over Villani in view of Gennaro. The Examiner's rejection in the Office Actions mailed January 11, 2000 and October 4, 2000 is summarized as follows:

> Villani motivates the combination of the antihistamine DCL with other medicinal agents in binary pharmaceutical compositions specifically embodied by the Gennaro reference. The substitution of DCL for an antihistamine and the substitution of a different analgesic substance is within the perview of the ordinary practitioner. While Villani does not specifically teach combinations of DCL with analgesics, Gennaro makes plain that such combinations are notoriously well known and accepted variations in the pharmaceutical composition art. *See* Office Actions at page 7-8.

These allegations are inaccurate and contrary to established law, as discussed below.

A. CLAIMS 48, 50, 52-53, AND 63-65 ARE NOT OBVIOUS

1. THE CITED REFERENCES DO NOT DISCLOSE OR SUGGEST ALL OF THE CLAIM LIMITATIONS RECITED BY THE PENDING CLAIMS

Claims 48, 50, 52-53, and 63-65 are directed, in part, to pharmaceutical compositions comprising from about 0.1 mg to about 5 mg of DCL, or a pharmaceutically acceptable salt thereof, an amount of a decongestant, and a pharmaceutically acceptable carrier.

The Examiner has the burden under § 103 to establish a *prima facia* case of obviousness. *In re Piasecki*, 745 F.2d 1468, 1471-1472 (Fed. Cir 1984). The Examiner can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references. *In re Lalu*, 747 F.2d 703, 705 (Fed. Cir.

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[6] Appellants reiterate that such a statement demonstrates the lack of anticipation by Villani alone as discussed above.

1984) ("in determining whether a case of *prima facie* obviousness exists, it is necessary to ascertain whether the prior art teachings would appear to be sufficient to one of ordinary skill in the art to suggest making the claimed substitution or other modification") (*Citing In re Taborsky*, 502 F.2d 775, 780 (CCPA 1974)). Moreover, "when determining the patentability of a claimed invention, which combines two known elements, the question is whether there is something in the prior art as a whole to suggest the desirability, and thus the obviousness, of making the combination." *In re Beattie*, 974 F.2d 1309, 1311-12 (Fed. Cir. 1992) (quoting *Lindemann Maschinenfabrik GmbH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1462 (Fed. Cir. 1984)). Moreover, the mere motivation in itself is not sufficient; to establish *prima facia* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981 (CCPA 1974); *See also In re Wilson*, 424 F.2d 1382, 1385 (CCPA 1970) (holding that all words in a claim must be considered in judging the patentability of that claim against the prior art). The mere fact that the combination of references could be modified is not legally sufficient. *See In re Gordon*, 733 F.2d 900 (Fed. Cir. 1984); *See also In re Lawkowski*, 871 F.2d 115 (Fed. Cir. 1989) ("holding that the mere fact that the prior art could be modified would not have made the modification obvious unless the prior art suggested the desirability of the modification").

The legally required suggestion in the references of all of the elements of the pending claims (*i.e.*, a pharmaceutical combination comprising from about 0.1 mg to 5 mg of DCL, or a pharmaceutically acceptable salt thereof, and an amount of a decongestant) is not present in Villani alone or in combination with Berkow. Specifically, Villani discloses a class of compounds, 7- and 8-(halo or trifluoromethyl)-substituted-6,11-dihydro-11-(4-piperidylidene)-5H-benzo[5,6]cyclohepta-[1,2-b]pyridines, in an *unspecified amount* ranging from 1 mg to 1000 mg in optional combination with an unspecified therapeutic agent (*i.e.*, "other therapeutic agents") such as a decongestant. Villani at col. 1, lines 17-38 and col. 8, lines 42-47. Villani does not disclose a pharmaceutical composition comprising the specific compound, DCL, in a specific range from about 0.1 mg to about 5.0 mg, much less a composition comprising from about 0.1 mg to about 5.0 mg of DCL and a decongestant.

Berkow does not remedy the deficiencies of Villani. Berkow merely discloses an antihistamine-decongestant composition containing the decongestant pseudoephedrine. Berkow at Page 326. However, Berkow does not disclose a specific antihistamine, much less a non-sedating antihistamine such as DCL. And Berkow certainly provides no indication of how much DCL should be used to provide a useful pharmaceutical composition. Significantly, Berkow does not provide any motivation to modify the disclosure of Villani.

In stark contrast, the claimed invention is a particular combination of a specific compound (*i.e.*, DCL) in a specific amount (*i.e.*, from about 0.1 mg to 5 mg), with another specific compound, which cannot be rendered *prima facia* obvious by such a generic disclosure. *See In re Jones* 958 F.2d 347, (Fed. Cir. 1992) (wherein the court found no

suggestion to combine the references to arrive at the claimed invention when the primary reference did not specifically teach the claimed compound and the secondary reference added nothing to cure the deficiencies of the primary reference). In addition, "the law is replete with cases in which the difference between the claimed invention and the prior art is some range or other variable within the claims." *In re Woodruff*, 919 F.2d 1575 (Fed. Cir. 1990). Villani discloses a range of a compound (*i.e.*, from 1 mg to 1000 mg) and provides no motivation to pick DCL from the compounds disclosed by Villani and combine this with a decongestant to obtain the claimed invention. Further, there is no teaching or suggestion of the specific claimed amount. The Examiner modifies the range of Villani without any teaching or suggestion in Villani to do so. By merely suggesting a range of "active ingredient" of from 1 mg to 1000 mg (*See* Villani at col. 8, lines 42-47), and by providing only examples wherein the amount of the single active ingredient is either 100 mg or 500 mg (*See, e.g.*, col. 22, lines 39 and 63), Villani teaches away from the very low amounts of DCL that are combined with another active ingredient as recited by the claims.

Thus, the invention recited by claims 48, 50, 52-53, and 63 is not obvious over Villani alone or in combination with Berkow because even their combination does not disclose all of the elements of the claims (*i.e.*, a pharmaceutical composition comprising the specific compound DCL in an amount of from about 0.1 mg to about 5 mg and a decongestant).

For this reason, the rejection of claims 64 and 65 under section 103 is even more inappropriate.

Claim 64 recites an aerosol and claim 65 recites an elixir each of which comprises DCL and an amount of decongestant. However, Villani does not disclose or suggest an aerosol or an elixir, much less an aerosol or elixir comprising DCL and a decongestant. And Berkow also does not disclose an aerosol or an elixir comprising a non-sedating antihistamine such as DCL in combination with a decongestant. Therefore, the references, taken alone or in combination, fail to disclose or suggest an aerosol or an elixir comprising DCL and a decongestant, and thus, the required suggestion of each of the claim limitations is absent from the references thereby rendering an obviousness rejection under section 103 is improper.

Because the Examiner improperly added limitations not disclosed in the references to allege an obviousness rejection, the Board should overturn the rejection of claims 48, 50, 52-53, and 63-65.

2. EVEN WITH THE USE OF HINDSIGHT THE CITED REFERENCES FAIL TO SUGGEST THE CLAIMED INVENTION

Specific compositions recited by the claims cannot be found in the cited art without the use of impermissible hindsight. In particular, the Examiner without any disclosure in the cited art contrives that which is recited by the pending claims to allege an obviousness rejection. However, obviousness "cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination." *ACS Hosp. Sys., Inc. v. Montefiore Hosp.*, 732 F.2d 1572, 1577 (Fed. Cir. 1984) (teachings of references can be combined only if there is some suggestion or incentive to do so). Here the prior art contains no such suggestion or motivation to combine the references. Instead the Examiner relies on hindsight in reaching his obviousness determination. The Federal Circuit has stated that when prior art references require selective combination to render obvious a subsequent invention, there must be some reason for the combination other than hindsight obtained from the invention itself. *Interconnect Planning Corp. v. Feil*, 774 F.2d 1132 (Fed. Cir. 1985). Moreover, when prior art references require selective combination to render obvious a subsequent invention, there must be some reason for the combination other than the hindsight obtained from the invention itself. *Interconnect Planning Corp. v. Feil*, 774 F.2d 1132 (Fed. Cir. 1985) (holding that it is error to reconstruct the patentee's claimed invention from the prior art by using the patentee's claim as a blueprint).

Even with the aid of impermissible hindsight the claimed pharmaceutical compositions comprising the specific combination of a specific amount of DCL and a decongestant cannot be identified from Villani alone or in combination with Berkow. Villani discloses broadly that a 7- or 8-(halo or trifluoromethyl)-substituted-6,11-dihydro-11-(4-piperidylidene)-5H-benzo[5,6]cyclohepta-[1,2-b]pyridine can be combined with another "therapeutic agent." Villani only discloses a class of compounds, 7- and 8-(halo or trifluoromethyl)-substituted-6,11-dihydro-11-(4-piperidylidene)-5H-benzo[5,6]cyclohepta-[1,2-b]pyridines, in an *unspecified amount* ranging from 1 mg to 1000 mg in optional combination with a second "therapeutic agent, such as a decongestant." Villani at col. 1, lines 17-38 and col. 8, lines 42-47. Villani does not specifically discloses a pharmaceutical composition comprising DCL and a decongestant, much less DCL in an amount from about 0.1 mg to 5 mg and a decongestant. By suggesting a range of "active ingredient" of from 1 mg to 1000 mg (Villani at col. 8, lines 42-47), and by providing only examples wherein the amount of the single active ingredient is either 100 mg or 500 mg (*See, e.g.*, col. 22, lines 39 and 63), Villani teaches away from the specific low amounts of DCL that are combined with another active ingredient as recited by the claims. *Monarch Knitting Mach. Corp. v. Sulzer Morat GmbH*, 139 F.3d 877, 885 (Fed. Cir. 1998). Moreover, only with the aid of impermissible hindsight could one of ordinary skill in the art ascertain that the small amounts

of one specific compound within the genus disclosed by Villani would have any usefulness when combined with a decongestant. *In re Gorman*, 933 F.2d 982 (Fed. Cir. 1991).

Berkow does not remedy the deficiencies of Villani. Berkow merely states that antihistamine-decongestant compositions were known in the art. Berkow at page 326. However, Berkow certainly provides no indication of a composition comprising DCL, or DCL and a decongestant, nor how much DCL should be used in a composition containing a decongestant. In sum, Berkow adds nothing to the '716 patent.

Claims 64 and 65 recite, in part, an aerosol spray and an elixir, respectively, which comprise an amount of DCL, or a pharmaceutically acceptable salt thereof, an amount of a decongestant.

Not even with the use of impermissible hindsight can one of ordinary skill in the art conjure from Villani and Berkow the aerosol or elixir as recited by claims 64 and 65, respectively. It is error to reconstruct the patentee's claimed invention from the prior art by using the patentee's claim as a "blueprint." The cited references alone or in combination do not disclose or suggest an aerosol or elixir, much less an aerosol or elixir comprising DCL and a decongestant.

Because Villani alone or in combination with Berkow does not disclose or suggest a pharmaceutical composition comprising from about 0.1 mg to about 5 mg of DCL and an amount of decongestant one skilled in the art would have had no motivation to make the compositions recited by claims 48, 50, 52-53, and 63. Moreover, because Villani alone or in combination with Berkow does not disclose or suggest an aerosol spray or an elixir comprising DCL and an amount of decongestant one skilled in the art would have had no motivation to make the compositions recited by claims 64 and 65. For the above reasons the rejections were in error and Appellants request that the Board reverse the rejection of claims 48, 50, 52-53, and 63-65 under § 103.

B. CLAIMS 54 AND 61 ARE NOT OBVIOUS

1. THE CITED REFERENCES DO NOT DISCLOSE OR SUGGEST ALL OF THE CLAIM LIMITATIONS RECITED BY THE PENDING CLAIMS

Claims 54 and 61 are directed to pharmaceutical compositions comprising from about 0.1 mg to about 5 mg of DCL, or a pharmaceutically acceptable salt thereof, an amount of a pseudoephedrine, and a pharmaceutically acceptable carrier.

The legally required suggestion of a pharmaceutical combination comprising DCL, or a pharmaceutically acceptable salt thereof, and pseudoephedrine is not present in Villani alone or in combination with Berkow. To be specific, Villani discloses a class of compounds, 7- and 8-(halo or trifluoromethyl)-substituted-6,11-dihydro-11-(4-piperidylidene)-5H-benzo[5,6]cyclohepta-[1,2-b]pyridines, in an *unspecified amount* ranging

from 1 mg to 1000 mg in optional combination with an unspecified therapeutic agent (*i.e.*, "other therapeutic agents") such as a decongestant. *See* Villani at col. 1, lines 17-38 and col. 8, lines 42-47. This is not sufficient to sustain a rejection under 35 U.S.C. § 103. *In re Lalu*, 747 F.2d 1468, 1471-1472 (Fed. Cir. 1984).

Berkow does not remedy the deficiencies of Villani. Berkow merely discloses an antihistamine-decongestant composition containing the decongestant pseudoephedrine. Berkow at Page 326. However, Berkow does not disclose a specific antihistamine, much less a non-sedating antihistamine such as DCL. Significantly, Berkow does not provide any motivation to modify the disclosure of Villani. Although, Berkow indicates that non-sedating antihistamines may be used, it provides no suggestion to use DCL in particular. In addition, Berkow merely states that "phenylpropanolamine, phenylephrine, and pseudoephedrine are available in antihistamine-decongestant preparations; however, absent the legally necessary suggestion to combine the references, the mere mention of such antihistamine-decongestant preparations does not legally support a case of *prima facia* obviousness.[7] *In re Vaeck*, 947 F.2d 488.

In contrast to the cited references, the claimed invention is a particular combination of specific compounds (*i.e.*, DCL and pseudoephedrine) in a specific amount (*i.e.*, from about 0.1 mg to 5 mg), which cannot be rendered *prima facia* obvious by such a generic disclosure of Villani (*i.e.*, "active compound" . . .and "other therapeutic reagents"). *See In re Baird* 16 F.3d 380 (Fed. Cir. 1994). *In re Jones* 958 F.2d 347 (Fed. Cir. 1992) (holding that the mere fact that a prior art genus contains a small number of members does not create a per se rule of obviousness. Some motivation to select the claimed species or subgenus must be taught by the prior art).

In sum, the invention as recited by claims 54 and 61 is not obvious over Villani alone or in combination with Berkow because neither reference provides a suggestion of a pharmaceutical composition comprising the specific compound DCL. *In re Oetiker*, 977 F.2d 1433 (Fed. Cir. 1992). Indeed, by suggesting a range of "active ingredient" of from 1 mg to 1000 mg (*See* Villani at col. 8, lines 42-47), and by providing only examples wherein the amount of the single active ingredient is either 100 mg or 500 mg (*See, e.g.*, col. 22, lines 39 and 63), Villani teaches away from the small amounts of DCL that are combined with another active ingredient as recited by the claims. *Gillette Co. v. S.C. Johnson & Son, Inc.*, 919 F.2d 720 (Fed. Cir. 1990). This can hardly be viewed as a suggestion to combine DCL with a decongestant in a manner as recited by the pending claims.

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[7] Berkow refers only to first generation or sedating antihistamines while the claimed invention is to non-sedating, second generation antihistamines.

2. EVEN WITH THE USE OF HINDSIGHT THE CITED REFERENCES FAIL TO SUGGEST THE CLAIMED INVENTION

As stated above, Villani only discloses a class of compounds, 7- and 8-(halo or trifluoromethyl)-substituted-6,11-dihydro-11-(4-piperidylidene)-5H-benzo[5,6]cyclohepta-[1,2-b]pyridines, in an *unspecified amount* ranging from 1 mg to 1000 mg in optional combination with a second "therapeutic agent," such as a decongestant. *See* Villani at col. 1, lines 17-38 and col. 8, lines 42-47. Villani does not specifically disclose a pharmaceutical composition comprising DCL, much less a pharmaceutical composition comprising the DCL with the specific decongestant pseudoephedrine. Thus, Villani is not sufficient to establish a rejection under 35 U.S.C § 103. *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 796 F.2d 443 (Fed. Cir. 1986).

Berkow does not remedy the deficiencies of Villani. Berkow merely discloses an antihistamine-decongestant composition containing the decongestant pseudoephedrine. Berkow at Page 326. However, Berkow does not disclose a specific antihistamine, much less a non-sedating antihistamine such as DCL. Although, Berkow suggests that non-sedating antihistamines may be used, it provides no suggestion to use DCL in particular. In addition, Berkow merely states that "phenylpropanolamine, phenylephrine, and pseudoephedrine are available in antihistamine-decongestant preparations;" however, absent the legally necessary suggestion to combine the references, the mere mention of such antihistamine-decongestant preparations does not legally support a case of *prima facia* obviousness. *ACS Hosp. Sys., Inc. v. Montefiore Hosp.*, 732 F.2d 1572, 1577 (Fed. Cir. 1984).

It is only with the impermissible aid of hindsight that the Examiner has contrived the Appellants compositions from the large number of compounds disclosed by Villani and Berkow, neither of which provide any suggestion for such a combination. *Interconnect Planning Corp. v. Feil*, 774 F.2d 1132 (Fed. Cir. 1985). Because this manner of concocting a *prima facia* rejection under § 103 is so clearly contrary to established law, Appellants submit that the rejection of claims 54 and 61 under § 103 must be withdrawn.

In sum, Villani alone or in combination with Berkow does not disclose or suggest a pharmaceutical composition comprising DCL and pseudoephedrine. Only using hindsight could one skilled in the art have had the suggestion to make the compositions recited by claims 54 and 61. Appellants therefore request that the rejection of claims 54 and 61 under § 103 be reversed by the Board.

C. CLAIMS 55, 57-59, 60-61, 66, AND 68 ARE NOT OBVIOUS

1. THE CITED REFERENCES DO NOT DISCLOSE OR SUGGEST ALL OF THE CLAIM LIMITATIONS RECITED BY THE PENDING CLAIMS

Claims 55, 57-59, 60-61, 66, and 68 are directed, *inter alia*, to pharmaceutical compositions comprising DCL, or a pharmaceutically acceptable salt thereof, non-steroidal anti-inflammatory agents, and a pharmaceutically acceptable carrier.

Villani discloses an "active compound" in optional combination with "other therapeutic agents," which encompass an undisclosed and a vast, if not infinite, number of compounds. *See* col. 8, lines 44-46. However, Villani does not specifically disclose non-steroidal anti-inflammatory agents, much less a specific example of a non-steroidal anti-inflammatory agent in combination with DCL as recited by claims 55, 57-59, 60-61, 66, and 68. Moreover, Villani does not disclose or suggest a pharmaceutical composition comprising the *specific* compound DCL, which is only one of the species encompassed by the genus disclosed by Villani, in combination with a non-steroidal anti-inflammatory agent. Further, when combined with the 7- or 8-(halo or trifluoromethyl)-substituted-6,11-dihydro-11-(4-piperidylidene)-5H-benzo[5,6]cyclohepta-[1,2-b]pyridines disclosed by Villani, the vast, if not infinite, number of "other therapeutic agents" does not even remotely suggest the specific combination of DCL and a non-steroidal anti-inflammatory agent, as recited by the pending claims. Thus, the required suggestion of a pharmaceutical composition comprising DCL and NSAIDs is clearly absent from Villani. *In re Lalu*, 747 F.2d 703, 705 (Fed. Cir. 1984).

Gennaro does not remedy the deficiencies of Villani. What the Examiner alleges as "Gennaro" is actually the Examiner picking and choosing from different chapters of the reference. The most pertinent section of Gennaro is page 1131, which discloses "Antihistamine Combinations." However, page 1131 only discloses antihistamine combinations containing first generation antihistamines with decongestants, analgesics, or anti-inflammatory agents. There is no suggestion of an antihistamine composition comprising a second generation antihistamine and an anti-inflammatory nor the required suggestion of the specific combination of DCL and a NSAID. The Federal Circuit has held time and again, "there must be some reason, suggestion, or motivation found in the prior art whereby a person of ordinary skill in the field of the invention would make the combination." *In re Oetiker*, 977 F.2d 1443, 1447 (Fed. Cir. 1992). Appellants do not dispute that NSAIDs were known (Gennaro does no more than evidence this fact) nor do Appellants dispute that first generation antihistamines have combined with other drugs, such as decongestants. However, this disclosure in Gennaro adds nothing of substance to Villani. In particular, even in combination with Genarro, Villani provides no suggestion of a pharmaceutical composition comprising DCL and a non-steroidal anti-inflammatory agent, as recited by claims 55, 57-59, 60-61, 66, and 68. *Northern Telecom, Inc. v. Datapoint Corp.*, 908 F.2d

931, 934 (Fed. Cir. 1990) (it is insufficient that prior art shows similar components, unless it also contains some teaching, suggestion, or incentive for arriving at the claimed structure).

Thus, because the combination of references does not generally disclose or suggest a second generation antihistamine and a non-steroidal anti-inflammatory agent, nor specifically disclose or suggest DCL and non-steroidal anti-inflammatory agent, or the specific non-steroidal anti-inflammatory agents recited by claims 57-59, the Board should reverse the rejection of claims 55, 57-59, 60-61, 66, and 68 under section 103.

2. EVEN WITH THE USE OF HINDSIGHT THE CITED REFERENCES FAIL TO SUGGEST THE CLAIMED INVENTION

The Examiner states that on page 7 of the October 4, 2000 Office Action that "Gennaro discloses numerous pharmaceutical compositions that contain antihistaminic activity on page 1131. . . with the following analgesic or antipyretic compounds on page 1110 (one of which is acetylsalicylic acid)." First, the Examiner is clearly using impermissible hindsight by using Appellant's disclosure to make a connection, where none exists, in Gennaro between salicylic acid and antihistamines. Second, as stated above, Genarro only discloses combinations of first generation antihistamines, known to cause sedation and other adverse-effects, with analgesics, decongestants, or anti-inflammatory agents. *See* Gennaro at page 1131, col. 2. Genarro fails to suggest a combination employing any second generation, non-sedating antihistamines, much less specifically employing DCL.

Appellants realize that the use of hindsight is very inviting here. However, even using hindsight to combine the references to combine the references in an attempt to arrive at the invention, Appellants assert that the combination at most suggests only that one of ordinary skill in the art "try" a pharmaceutical composition comprising an analgesic, decongestant, or NSAID and one of the compounds disclosed by Villani. As the Board is aware, this is not the proper legal standard for obviousness. *In re O'Farrell*, 853 F.2d 894.

In sum, the combination of Villani and Genarro requires one of ordinary skill in the art to impermissibly use hindsight to "pick and choose" unconnected sections of Genarro and then combine those without motivation or suggestion with unrelated passages of Villani. *In re Fine*, 837 F.2d 1071 (Fed. Cir. 1988).

Even then, this combination of cited references may only be considered to suggest that one of ordinary skill in the art try a pharmaceutical composition comprising a an analgesic or anti-inflammatory and one of the number of compounds disclosed by Villani. Thus, at best, Villani and Genarro render a more general combination of DCL and an anti-inflammatory "obvious to try." This is not, however, the proper test of obviousness. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1380 (Fed. Cir.1986).

Appellants therefore submit that the rejection of claims 55, 57-59, 60-61, 67 and 68 under U.S.C. § 103(a) should be withdrawn.

D. CLAIMS 56, 60-61, 67, AND 68 ARE NOT OBVIOUS

1. THE CITED REFERENCES DO NOT DISCLOSE OR SUGGEST ALL OF THE CLAIM LIMITATIONS RECITED BY THE PENDING CLAIMS

Claims 56, 60-61, 67, and 68 are directed, in part, to pharmaceutical compositions comprising descarboethoxyloratidine, or a pharmaceutically acceptable salt thereof, a non-narcotic analgesics, and a pharmaceutically acceptable carrier. More specifically, these claims recite the following specific combinations: a pharmaceutical composition comprising descarboethoxyloratadine, or a pharmaceutically acceptable salt thereof, acetaminophen, and a pharmaceutically acceptable carrier

Again, Villani merely discloses an "active compound" in optional combination with "other therapeutic agents." Villani does not specifically disclose or suggest the use of any active compound in combination with a non-narcotic analgesic as recited in claims 56, 60-61, 67 and 68.

As stated above, Gennaro only discloses antihistamine combinations containing first-generation, sedating antihistamines with decongestants, analgesics, or anti-inflammatory agents. There is no suggestion of an antihistamine composition comprising a second generation antihistamine such as DCL, much less a composition comprising DCL and a non-narcotic analgesic. The Federal Circuit has held time and again, "there must be some reason, suggestion, or motivation found in the prior art whereby a person of ordinary skill in the field of the invention would make the combination." *In re Oetiker*, 977 F.2d 1443, 1447 (Fed. Cir. 1992). Appellants do not dispute that non-narcotic analgesics were known (Gennaro does no more than evidence this fact). However, this disclosure in Gennaro adds nothing of substance to Villani. Much less provide the required suggestion or motivation to combine the references.

Assuming *arguendo* that there was a motivation to combine the two references, their combination at most only suggests that one of ordinary skill in the art "try" a pharmaceutical composition comprising a non-narcotic analgesic and one of the compounds disclosed by Villani.[8] However, it is well established that an allegation that a claimed invention may have been "obvious to try" does not establish a case of *prima facia* obviousness. *See Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F2d 1367, 1380 (Fed. Cir. 1986) (holding invitations to try. . . do not show obviousness since they "do not suggest how that end might be accomplished").

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[8] Appellants reiterate that no such suggestion actually exists in the combination of references.

2. EVEN WITH THE USE OF HINDSIGHT THE CITED REFERENCES FAIL TO SUGGEST THE CLAIMED INVENTION

Using impermissible hindsight, the Examiner states that on page 7 of the October 4, 2000 Office Action that "Gennaro discloses numerous pharmaceutical compositions that contain antihistaminic activity on page 1131. . . with the following analgesic or antipyretic compounds on page 1110 (one of which is acetylsalicylic acid)." Genarro merely discloses combinations of first generation antihistamines, known to cause sedation and other adverse-effects, with mild analgesics. *See* Gennaro at page 1131, col. 2. Genarro fails to disclose any second generation, non-sedating antihistamines, much less to specifically disclose DCL in combination with an additional specific active ingredient.

To arrive at something close to the invention, the combination of Villani and Genarro requires one of ordinary skill in the art to impermissibly "pick and choose" from the disclosure of Genarro and then combine that with an unrelated disclosure of Villani. This is only possible when using the present claims as a blueprint (*i.e.*, using impermissible hindsight). Appellants therefore submit that the rejection of claims 55, 60, and 61 under U.S.C. § 103(a) should be withdrawn.

In sum, even in combination Villani and Genarro do not provide the required suggestion of a pharmaceutical composition comprising DCL and acetaminophen, as recited by claims 56, 60, and 61. Assuming *arguendo* that there was a motivation to combine the two references, their combination, at most, suggests that one of ordinary skill in the art try a pharmaceutical composition comprising a mild analgesic and one of the compounds disclosed by Villani. Clearly, this suggestion does not arrive at the claimed invention, much less provide a reasonable expectation of its success. Therefore, Appellants submit that the rejection of claims 56, 60, and 61 under U.S.C. § 103(a) should reversed by the Board.

CONCLUSION

For the reasons stated above, it is respectfully submitted that the final rejections of claims under 35 U.S.C. § 102(b) and § 103 are in error and warrant reversal by the Board.

Respectfully submitted,

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